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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/859,439	05/18/2001	Indra Prakash	2047.154	3715

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EXAMINER
ZUCKER, PAUL A

ART UNIT	PAPER NUMBER
1621	14

DATE MAILED: 05/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/859,439	PRAKASH, INDRA	
	Examiner	Art Unit	
	Paul A. Zucker	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,14 and 16-20* is/are rejected.

7)☒ Claim(s) *10-13 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 28 April 2003 has been entered.

Current Status

2. This action is responsive to Applicants' amendment of 28 April 2003 in Paper No 13.
3. Receipt and entry of Applicants' amendment is acknowledged.
4. Claims 1-20 remain pending.
5. Applicant's declaration has been carefully considered but was not foun persuasive for the reasons discussed below.

New Objections and Rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

6. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 recites the limitations "dimethyl or diethyl acetals of

hexafluoroacetone, hexachloroacetone, and combinations thereof" in lines 2-3.There is insufficient antecedent basis for these limitations in the claim.

Claim Rejections - 35 USC § 103

7. Claims 1, 2, 4-9, 14 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burger et al (Chemmiker Zeitlung 1990, 114(7-8), pages 249-251) and further in view of Claude et al (US 5,510,508 04-1996).

Instantly claimed is a process for the synthesis of N-[N-(3,3-dimethylbutyl)-L-α-aspartyl-L-phenylalanine-1-methyl ester (neotame) via: a) the formation of an oxazolidinone from N-[N-(3,3-dimethylbutyl)-L-α-aspartic acid from acarbonyl compound or its equivalent, followed by b) reacting the oxazolidinone with phenylalanine methyl ester to yield neotame.

Burger teaches (Page 250, left column, lines 17-34) the synthesis of oxazolidinones of general structure 3 (Page 249, upper right-hand column) which, with n=1 (compound 3a), corresponds to that derived from aspartic acid. The amino acid (100 mmol) in anhydrous dimethylsulfoxide is vigorously stirred at room temperature and a gaseous stream of hexafluoroacetone is introduced. The introduction of hexafluoroacetone is stopped when its uptake ceases and reflux is noted. Thus while Burger is silent with respect to the reactant ratios it reasonable to assume the instant claimed slight excess (1:1.1-1.4) of hexafluoroacetone is present. Reaction is continued for 2-3 hours to give the crystalline oxazolidinone after work-up. Burger

further teaches (Page 250, last 5 lines of left column- first 9 lines of right column) the aminolysis of the oxazolidinones to form dipeptides such as aspartame. The oxazolidinone (20 mmol) in anhydrous ether is slowly added with stirring at room temperature to a solution of phenylalanine methyl ester (24 mmol) in anhydrous ether (corresponding to 1:1.2 ratio of oxazolidinone:phenylalanine) and reaction continued for 24 hr to give a 72% yield of aspartame.

Burger is silent with respect to application of his process to the synthesis of neotame.

Claude, however, teaches (Column 1, lines 1-42) the structure of neotame, an artificial sweeter closely related in structure to aspartame. The closeness of the relationship between these two compounds is underscored by the fact that Claude further discloses (Column 3, line 63 – column 4, line 40) the synthesis of neotame in one step from aspartame.

Thus the instantly claimed process would have been obvious to one of ordinary skill in the art. The motivation would have been to apply the efficient process disclosed by Berger for the synthesis of aspartame, a commercially important artificial sweetener, to the synthesis of the aspartame derivative, neotame. There would have been a reasonable expectation for success because aspartame contains the same functional core as neotame and would therefore be expected to react with ketones in a similar fashion.

Response to Applicant's Remarks with Regard to This Rejection

8. Applicant presents several arguments to which the Examiner responds below:

    a. Applicant references arguments already of record and the Examiner, in reply, references his response to those arguments.

    b. Applicant further argues that the structural differences between aspartame and neotame, and the starting materials for their production, are so great that one of ordinary skill in the art would not have had a reasonable expectation of success. In support of this assertion Applicant argues that aldehydes cannot be used to synthesize neotame while the ketones can. Applicant further provides a declaration that states the same. The Examiner makes three points with regard to this argument:

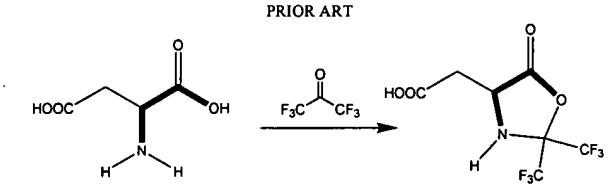
        i. There is no evidence in the prosecution history of this application that supports the assertion that aldehydes can be used in the synthesis of aspartame via a process analogous to that taught by Burger. Burger teaches only the use of hexafluoroacetone as a carbonyl component. Applicant has not provided any evidence to support the assertion that aldehydes may be used to replace the ketone taught by Burger.

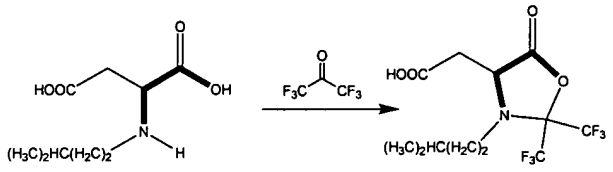
        ii. Because the prior art of record teaches only the use of ketones, the differences in behavior with aldehydes of the starting materials for the synthesis of aspartame and neotame does not appear to be particularly relevant in this context. The starting materials for the synthesis of aspartame and neotame are different compounds, having

different chemical structures, and are thus expected to exhibit different chemical behaviors. Those differences would not, however, prevent a reasonable expectation of success in the application of the process of Burger to the synthesis of neotame.

iii. The differences between the prior art process and Applicant's are shown below:

PRIOR ART





INVENTION

Applicant's general statements to the effect that the starting compounds have different properties do not shed light on why one of ordinary skill in the art would have not had a reasonable expectation of success. All the required features (shown in bold above) for reaction are present. The additional substitution found on the nitrogen atom in the starting material for the synthesis of neotame (INVENTION) is simply a spectator and does not participate in any direct fashion in the process. Since all the required atoms are present in the proper arrangement, one of ordinary skill in the art would have had a reasonable expectation of success.

Applicant's arguments filed 28 April 2003 have been fully considered but they are not persuasive for the reasons given above.

Claim Objections

9. Claims 10, 11-13 and 15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Allowable Subject Matter

10. Claims 10-13 and 15 are drawn to allowable subject matter. The following is a statement of reasons for the indication of allowable subject matter: The closest art of record, Burger et al (Chemmiker Zeitlung 1990, 114(7-8), pages 249-251) neither discloses nor fairly suggests the limitations of claims 3, 10,11,13, 15. No suggestion exists that acetals in the presence of pyridinium p-toluenesulfonate or p toluenesulfonic acid can substitute for hexafluoracetone or that the oxazolidinone formation and aminolysis can be carried out in the same solvent. Burger also does not suggest that additional acid (beyond that provided by the starting material) be added.

Conclusion

11. Claims 1-20 remain pending. Claims 1-9, 14 and 16-20 are rejected. Claims 10-13 and 15 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 703-306-0512. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Paul A. Zucker
Patent Examiner
Technology Center 1600

April 30, 2003

Johann Richter, Ph.D., Esq.
Supervisory Patent Examiner
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